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Amendments to the Claims:

612-455-3801

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

1. (Previously presented) An isolated or synthesized polypeptide, wherein the polypeptide is a fragment of a Notch protein,

N-terminal of the polypeptide is Site-2 cleavage site of the Notch protein that is positioned near a surface of cell membrane,

C-terminal of the polypeptide is Site-4 cleavage site of the Notch protein that is positioned on N-terminal side in a transmembrane domain of the Notch protein relative to Site-3 cleavage site, wherein the Site-3 cleavage site is positioned at either inside the cell membrane or in close proximity to the cell membrane inside the cell,

the polypeptide comprises at least a part of the transmembrane domain of the Notch protein,

the polypeptide is produced and released to an extracellular space as a result of proteolysis at the Site-4 cleavage site that occurs simultaneously with, before, or after proteolysis at the Site-3 cleavage site, wherein the proteolysis at the Site-3 cleavage site occurs subsequent to proteolysis at the Site-2 cleavage site and translocates Notch intracellular cytoplasmic domain (NICD) to a nucleus of the cell, and

the Notch protein is a Notch protein that exists in an at least one organism selected from the group consisting of a human, a mouse, a rat, a rabbit, a goat, a swine, a bovine, a drosophila, and a nematode.

- 2. (Original) The polypeptide according to claim 1, which is released to the extracellular space in proportion to Notch signal transduction.
- 3. (Previously Presented) The polypeptide according to claim 1, wherein the release of the polypeptide to the extracellular space results from presentilin-dependent proteolysis.
- 4-5. (Cancelled)

- 6. (Withdrawn currently amended) An isolated or synthesized polypeptide emprising consisting of an amino acid sequence of at least one of SEQ ID NOS: 1 to 18.
- 7. (Withdrawn currently amended) An isolated or synthesized polypeptide comprising consisting of an amino acid sequence of at least one of SEQ ID NOS: 1 to 18 in which one or several of amino acids are deleted, substituted, or inserted, wherein the polypeptide is a fragment of a Notch protein,

N-terminal of the polypeptide is Site-2 cleavage site of the Notch protein that is positioned near a surface of cell membrane,

C-terminal of the polypeptide is Site-4 cleavage site of the Notch protein that is positioned on N-terminal side in a transmembrane domain of the Notch protein relative to Site-3 cleavage site, wherein the Site-3 cleavage site is positioned at either inside the cell membrane or in close proximity to the cell membrane inside the cell,

the polypeptide comprises at least a part of the transmembrane domain of the Notch protein,

the polypeptide is produced and released to an extracellular space as a result of proteolysis at the Site-4 cleavage site that occurs simultaneously with, before, or after proteolysis at the Site-3 cleavage site, wherein the proteolysis at the Site-3 cleavage site occurs subsequent to proteolysis at the Site-2 cleavage site and translocates (Notch intracellular cytoplasmic domain (NICD) to a nucleus of the cell, and

the Notch protein is a Notch protein that exists in an at least one organism selected from the group consisting of a human, a mouse, a rat, a rabbit, a goat, a swine, a bovine, a drosophila, and a nematode.

- 8. (Withdrawn) The polypeptide according to claim 7, which is released to the extracellular space in proportion to a Notch signal.
- 9. (Withdrawn) The polypeptide according to claim 7, wherein the release of the polypeptide to the extracellular space results from presentilin-dependent proteolysis.

- 10. (Withdrawn) A biomarker comprising the polypeptide according to claim 1.
- 11. (Withdrawn) The biomarker according to claim 10 for detecting at least one selected from the group consisting of Notch signal transduction, cell differentiation, tumor, apoptosis, and Alzheimer's disease.
- 12. (Withdrawn) An antibody that can recognize the polypeptide according to claim 1.
- 13. (Withdrawn previously presented) The antibody according to claim 12, which is at least one of a monoclonal antibody and a polyclonal antibody.
- 14. (Withdrawn) A reagent for detecting at least one selected from the group consisting of Notch signal transduction, cell differentiation, tumor, apoptosis, and Alzheimer's disease, which comprises the antibody according to claim 12.
- 15. (Withdrawn previously presented) A gene encoding the polypeptide according to claim 1.
- 16. (Withdrawn) The gene according to claim 15, which is DNA or RNA.
- 17. (Withdrawn previously presented) A vector comprising the gene according to claim 15.
- 18. (Withdrawn) A transformant transformed with the vector according to claim 17.
- 19. (Previously presented) The polypeptide according to claim 1, wherein an amino acid sequence of the polypeptide is at least one selected from the group consisting of SEQ ID NOS: 1 to 18.
- 20. (Previously presented) The polypeptide according to claim 1, wherein an amino acid sequence of the polypeptide is at least one selected from the group consisting of SEQ ID NOS: 1 to 18 in which one or several of amino acids are deleted, substituted, or inserted.

21. (Previously presented) The polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence at least one selected from the group consisting of

an amino acid sequence consisting of the 1st residue to the 8th residue of SEQ ID NOS: 37 and 38, and

an amino acid sequence consisting of the 1^{st} residue to the 6^{th} residue of SEQ ID NOS: 39 to 44.